62. (new) The isolated nucleic acid molecule of claim 52, wherein said isolated human Bcl-xL binding protein fragment modulates apoptosis.

63. (new) The isolated nucleic acid molecule of claim 62, wherein said isolated human Bcl-xL protein fragment comprises from about amino acid 419 to about amino acid 549 of SEQ ID NO:2.

D3

64. (new) The isolated nucleic acid molecule of claim 62, wherein said isolated human Bcl-xL protein fragment comprises from about amino acid 429 to about amino acid 559 of SEQ ID NO:2.

65. (new) An isolated nucleic acid molecule comprising a nucleotide sequence, wherein said isolated human Bcl-xL binding protein has greater than 91% nucleic acid sequence identity with a Bcl-xL binding protein set forth in SEQ ID NO:1.

Remarks

Claims 62-65 have been added by this amendment. The claims are 43-44 and 49-65. New claim 62 finds support in Example 6, pages 99-100. New claim 63 finds support at page 9 lines 18-19 of the application as well as in Example 6, pages 99-100. New claim 64 finds support at page 9 lines 18-20 of the application as well as in Example 6, pages 99-100. New claim 65 finds support at page 19 lines 9-10, page 20 line 2, and page 22 line 17. This amendment contains no new subject matter.

Response to Rejection Under 35 U.S.C. §102(b)

Claims 43-44 have been rejected at page 2 under 35 U.S.C. §102(b) (citing MPEP 2121.02) as having been disclosed by Nagase et al. (*DNA Res.*, 3:321-329, 1996) (hereinafter "Nagase"). Applicants respectfully traverse and request that the Examiner reconsider and withdraw this rejection. To anticipate, a reference must provide an enabling disclosure. The MPEP states at 2121.01:

> "In determining that quantum of prior art disclosure which is necessary to declare an applicant's invention 'not novel' or anticipated' within section 102, the stated test is whether a reference contains an 'enabling disclosure'… ." *In re Hoekssema*, 399 F.ed 269, 158 USPQ 596 (CCPA 1968).

Nagase merely names the claimed sequence. He does not provide an enabling disclosure of the instant invention. No use for the invention was known until revealed by the present

application. Nagase does not suggest that a nucleic acid molecule (SEQ ID NO:1) encoding a protein of SEQ ID NO:2 would bind Bcl-xL or modulate apoptosis in mammalian cells. In fact, Nagase provides no use for the bare sequence of the nucleic acid molecule disclosed (Declaration of Brad Ozenberger pages 3-5, March 1, 2002).

In Adang v. Fischhoff, 286 F.3d 1346 (Fed. Cir. April 10, 2002), the standard for enablement is very strict. Adang v. Fischhoff was cited at page 1355 as lacking enablement because of "'substantially unpredictable' art as of the filing date":

> The legal question of enablement involves an assessment of whether a patent disclosure would have enabled one of skill in the art at the time the application was filed to make and use the claimed invention without undue experimentation. (Emphasis added)

Although Adang documented successful experimentation involving tobacco plants, they did not enable the transformation of the protein in other species as part of the invention. Nagase does not suggest any use. Nagase merely reveals the putative sequence (analogous to a name) of a chemical.

Concerning the Examiner's comment at page 3 of the Office Action (paper 21) that Nagase discloses that KIAA0269 has homology to genes that play key roles in regulation, Applicants respectfully state that the Examiner misunderstands the Applicants' earlier argument (Preliminary Amendment and Response to Final Office Action Mailed November 16, 2001, filed March 12, 2002). As stated in the Declaration Under 37 C.F.R. §1.132 from March 1, 2002 (a courtesy copy accompanies this Response), the abstract of Nagase contains a general statement of function that is not supported in the body of the article for the specific cDNA clone KIAA0269 which corresponds to SEQ ID NO:1 of the instant invention. The only statement which could be said to suggest function (certainly not any suggestion of use) for KIAA0269 in Nagase is at page 324 in Table 1 where KIAA0269 is shown to have 29.9% homology with an extensin-like protein from *Zea mays*. Nagase has clearly not disclosed any enabling use for KIAA0269.

At page 3 the Examiner states that, "prior art is not required to be useful to anticipate." Applicants respectfully point out that it is well-established law that for a reference to anticipate an invention, it has to be enabling. 35 U.S.C. §112 paragraph 1 defines enablement as including "the manner and process of making and using [the invention]." In Elan Pharmaceuticals, Inc. v. Mayo Foundation for Medical Education and Research, 304 F.3d 1221, (Fed. Cir. Aug. 30, 2002), it is stated at page 1229:

> No doctrine of the patent law is better established than that a prior patent or other publication to be an anticipation must bear within its four corners adequate directions for the practice of the patent invalidated. If the earlier disclosure offers no more than a starting point for further experiments, if its teaching will sometimes succeed and sometimes fail, if it does not inform the art without more how to practice the new invention, it has not correspondingly enriched the store of common knowledge, and it is not an anticipation. (Emphasis added)

Response to Rejection Under 35 U.S.C. §112 Paragraph 1

The Examiner has rejected claims 49-53 and 57-59. In light of Applicants' current amendment to claims 49-56, it is believe that this rejection is moot.

Applicants respectfully traverse the Examiner's rejection of claim 53 at page 4 wherein the Examiner states that the claim does not "specify the exact site for binding." The Examiner has provided no evidence to support this assertion. As stated in the application on page 9, "Preferred Bcl-xL binding domains are approximately 120-150 amino acid residues in length." Further, "...Pablo Bcl-xL binding domain comprises from about amino acid 419 to about amino acid 559 or about amino acid 429 to about amino acid 559 of SEQ. ID NO:2." Applicant suggests that the Examiner consider this argument in light of In re Sang-Su Lee, 277 F.3d 1338 (Fed. Cir. Jan. 18, 2002) at page 1345:

> "Common knowledge and common sense," even if assumed to derive from the agency's expertise, do not substitute for authority when the law requires authority.

Applicants respectfully maintain that the Examiner misstates the evidence in his statement at page 4 that "no information is given regarding a methodology to determine [binding

domains]." On page 9 lines 23-30 of the application, Applicants state, "With respect to Bcl-xL binding domains, the term 'isolated Bcl-xL binding domain' includes domains which are isolated or separated from the amino acid residues which comprise the full length Bcl-xL binding molecule, such as Pablo. For example a nucleic acid molecule encoding an isolated Pablo Bcl-xL binding domain consists of that portion of a Pablo nucleic acid molecule encoding the Bcl-xL binding domain of a Pablo protein." In addition, Example 6 on page 99 starting at line 10, titled, "Identification of the Bcl-xL Binding Region of Pablo" provides a specific example of how a binding region may be found.

Regarding the Examiner's rejection of claim 50 at pages 4-5 pursuant to 35 U.S.C. §112 paragraph 1 because of the "hybridization" language, Applicants respectfully refer the Examiner to the PTO Synopsis of Application of Written Description Guidelines. Therein the PTO states at page 36 that an invention is adequately described when, "...the essential feature of the claimed invention is the isolated nucleic acid that hybridizes to SEQ ID NO: 1 under highly stringent conditions and encodes a protein with a specific function." Their example of "highly stringent hybridization conditions," at page 38 is "6XSSC and 65 degrees Celsius."

Claim 50 meets these requirements, which were approved by the Court of Appeals for the Federal Circuit in Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316, (Fed. Cir. July 15, 2002). Claim 50 states that the "...nucleotide sequence hydridizes to the complement of a nucleotide sequence set forth in SEQ ID NO: 1 which encodes a Bcl-xL binding protein..." under the highly stringent conditions of "...6X SSC at 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 50-65°C."

As stated in Enzo at page 1327:

> ...claims to nucleic acids based on their hybridization properties...may be adequately described if they hybridize under highly stringent conditions to known sequences because such conditions dictate that all species within the genus will be structurally similar.

Applicants respectfully traverse the Examiner's objection at page 5 of Claim of "85% language." We have amended claim 49 to 98% sequence identity and believe that the objection is moot (see also the Declaration Under 37 C.F.R. §1.132 from November 4, 2002).

Conclusion

It is the Applicants' belief that the pending claims are in condition for allowance, and action towards that effect is respectfully requested. If there are any matters which may be resolved or clarified through a telephone interview, the Examiner is requested to contact the undersigned attorney at the number indicated.

CERTIFICATE OF MAILING 37 CFR §1.10

I hereby certify that this paper and the documents referred to as enclosed therein are being deposited with the United States Postal Service on the date written below in an envelope as "Express Mail Post Office to Addressee" Mailing Label Number EL 95385302 US addressed to the Commissioner for Patents, Washington, DC 20231.

11/4/02
Date

Elizabeth Ruzich
Elizabeth Ruzich

Gavin T. Bogle

Limited Recognition Under 37 C.F.R. §10.9(b)

Wyeth
Patent Law Department
Five Giralda Farms
Madison, NJ 07940-0874
Tel. No. (617) 665-8079

Claims Marked to Show Changes

49. (amended) An isolated nucleic acid molecule comprising a nucleotide sequence encoding an isolated [mammalian]human Bcl-xL binding protein, wherein said isolated [mammalian]human Bcl-xL binding protein has [85]98% amino acid sequence identity with a Bcl-xL binding protein set forth in SEQ ID NO:2.

50. (amended) An isolated nucleic acid molecule comprising a nucleotide sequence encoding an isolated [mammalian]human Bcl-xL binding protein, wherein said nucleotide sequence hybridizes to the complement of a nucleotide sequence set forth in SEQ ID NO:1 which encodes a Bcl-xL binding protein in 6X SSC at 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at 50-65°C.

51. (amended) An isolated nucleic acid molecule comprising a nucleotide sequence encoding an isolated [mammalian]human Bcl-xL binding protein as shown in SEQ ID NO:1.

52. (amended) A nucleic acid molecule comprising a nucleotide sequence encoding an isolated [mammalian]human Bcl-xL binding domain, wherein said domain is a fragment of the nucleic acid molecule [of claim 51]as shown in SEQ ID NO:1.

54. (amended) [The]An isolated nucleic acid molecule [of claim 49]comprising a nucleotide sequence encoding an isolated human Bcl-xL binding domain, wherein said isolated [mammalian]human Bcl-xL binding protein modulates apoptosis.

55. (amended) The isolated nucleic acid molecule of claim 50, wherein said isolated [mammalian]human Bcl-xL binding protein modulates apoptosis.

56. (amended) The isolated nucleic acid molecule of claim 51, wherein said isolated [mammalian]human Bcl-xL binding protein modulates apoptosis.

62. The isolated nucleic acid molecule of claim 52, wherein said isolated human Bcl-xL binding protein fragment modulated apoptosis.

63. The isolated nucleic acid molecule of claim 62, wherein said isolated human Bcl-xL protein fragment comprises from about amino acid 419 to about amino acid 549 of SEQ ID NO:2.

64. The isolated nucleic acid molecule of claim 62, wherein said isolated human Bcl-xL protein fragment comprises from about amino acid 429 to about amino acid 559 of SEQ ID NO:2.

65. An isolated nucleic acid molecule comprising a nucleotide sequence, wherein said isolated human Bcl-xL binding protein has greater than 91% nucleic acid sequence identity with a Bcl-xL binding protein set forth in SEQ ID NO:1.